NATIONAL GUIDELINE CLEARINGHOUSE™ (NGC)
GUIDELINE SYNTHESIS

SCREENING FOR PROSTATE CANCER

Guidelines

1. American Cancer Society (ACS). Recommendations from the American Cancer Society Workshop on Early Prostate Cancer Detection, May 4-6, 2000 and ACS guideline on testing for early prostate cancer detection: update 2001. CA Cancer J Clin 2001 Jan-Feb;51(1):39-44 [181 references].
2. New University of Michigan Health System (UMHS). Adult preventive health care: cancer screening. Ann Arbor (MI): University of Michigan Health System; 2004 May. 12 p. [4 references].
3. U.S. Preventive Services Task Force (USPSTF). Screening for prostate cancer: recommendations and rationale. Ann Intern Med 2002 Dec 3;137(11):915-6 [8 references].

INTRODUCTION:

A direct comparison of the American Cancer Society, (ACS), the University of Michigan Health System (UMHC), and the U.S. Preventive Services Task Force (USPSTF) guidelines on screening for prostate cancer is provided in the following tables. The supporting evidence is classified and identified with the major recommendations from the UMHS and USPSTF. The definitions of their rating schemes are included in the last rows of Table 2.

Following the content comparison, areas of agreement and differences among the guidelines are discussed.

Abbreviations:

- ACS, American Cancer Society
- DRE, digital rectal examination
- PSA, prostate specific antigen
- UMHS, University of Michigan Health System
- USPSTF, U.S. Preventive Services Task Force

TABLE 1: COMPARISON OF SCOPE AND CONTENT	
ACS (2001)	Objectives • To update the 1997 American Cancer Society guideline pertaining

	to prostate cancer screening. • To offer recommendations to health care professionals and the public for informed decision-making related to early detection of prostate cancer Interventions and Practices Considered • DRE • PSA Target Population • Men aged 50 years and older who have a life expectancy of at least 10 years and younger men who are at high risk for prostate cancer • Men aged 45 years and older of Sub-Saharan African descent or with first-degree relative diagnosed at a young age • Men 40 and older with multiple first-degree relatives diagnosed with prostate cancer at an early age
UMHS (2004) New	Objectives • To implement an evidenced-based strategy for cancer screening in adults Interventions and Practices Considered • DRE • PSA Target Population • Men >age 50 • Men with positive family history and for African Americans, consider starting PSA screening at age 40
USPSTF (2002)	Objectives • To summarize the current USPSTF recommendations on screening for prostate cancer and the supporting scientific evidence • To update the 1996 recommendations contained in the Guide to Clinical Preventive Services, second edition Interventions and Practices Considered • DRE

	• PSA Target Population • Men aged 50-70 years who are at average risk • Men over age 45 who are at increased risk (African American men and men with a family history of a first-degree relative with prostate cancer)

TABLE 2: COMPARISON OF RECOMMENDATIONS FOR PROSTATE CANCER SCREENING	
ACS (2001)	Targeted screening/Screening tests/Informed decision-making ACS recommends that both the PSA test and the DRE should be offered annually beginning at age 50, to men who have a life expectancy of at least 10 years. Men at high risk should begin testing at age 45. Information should be provided to patients about benefits and limitations of testing. Specifically, prior to testing, men should have an opportunity to learn about the benefits and limitations of testing for early prostate cancer detection and treatment. High-risk groups include men of African descent (specifically, sub-Saharan African descent) and men with a first-degree relative diagnosed at a young age. Risk increases with the number of first-degree relatives affected by prostate cancer.
UMHS (2004) New	Modality. PSA and DRE. Both have specificity limitations. Initiate. Clinicians who screen for prostate cancer should share decision making with patients [A], giving objective information about the potential risks and benefits of screening. • Average risk. For men >age 50, consider initiating PSA screen. • High-risk. For men with positive family history and for African Americans, consider starting PSA screening at age 40 [D]. Frequency. Annually Terminate. Stop when life expectancy is less than 10 to 15 years [C]. There is considerable controversy surrounding screening for prostate cancer. Early detection and treatment may avert future prostate cancer-related illness, but treatment includes some risk of sexual dysfunction and incontinence and a small risk of treatment-induced mortality. At this time, no trials of sufficient power are available to

	document the benefit of aggressive treatment (e.g. surgery, radiation) versus conservative management and hormonal therapy. Similarly, there is no conclusive evidence that routine screening for prostate cancer is beneficial, and there is no consensus concerning the role of DRE and PSA testing in screening.
USPSTF (2002)	Routine screening USPSTF concludes that the evidence is insufficient to recommend for or against routine screening for prostate cancer using PSA testing or DRE. I recommendation. The USPSTF found good evidence that PSA screening can detect early-stage prostate cancer but mixed and inconclusive evidence that early detection improves health outcomes. Screening is associated with important harms, including frequent false-positive results and unnecessary anxiety, biopsies, and potential complications of treatment of some cancers that may never have affected a patient's health. The USPSTF concludes that evidence is insufficient to determine whether benefits outweigh harms for a screened population. Clinical Considerations • PSA testing and DRE can effectively detect prostate cancer at early pathologic stages. There is insufficient evidence, however, that the currently available treatments (radical prostatectomy, radiation therapy, or hormonal therapy) reduce morbidity and mortality from early prostate cancer. Therefore, the benefit of screening for and treating early prostate cancer is unknown. Informed decision-making/Targeted screening/Screening tests/Screening frequency Clinical Considerations • Despite the absence of firm evidence of effectiveness, some clinicians may opt to perform screening for other reasons. Given the uncertainties and controversy surrounding prostate cancer screening, clinicians should not order the PSA test without first discussing with the patient the potential but uncertain benefits (reduction of morbidity and mortality from prostate cancer) and the possible harms (false-positive results, unnecessary biopsies, and possible complications of treatment) of prostate cancer screening. Men should be informed of the gaps in the evidence, and they should be assisted in considering their personal preferences and risk profile before deciding whether to be tested. • If early detection improves health outcomes, the population most likely to benefit from screening will be men aged 50-70 years who are at average risk, and men over age 45 who are at increased risk (African American men and men with a family history of a first-degree relative with prostate cancer). Benefits may be

	smaller in Asian Americans, Hispanics, and other racial and ethnic groups that have a lower risk of prostate cancer. Older men and men with other significant medical problems who have a life expectancy of fewer than 10 years are unlikely to benefit from screening. • PSA testing is more sensitive than DRE for the detection of prostate cancer. PSA screening with the conventional cut-point of 4.0 ng/dl detects a large majority of prostate cancers; however, a significant percentage of early prostate cancers (10-20%) will be missed by PSA testing alone. Using a lower threshold to define an abnormal PSA detects more cancers at the cost of more false positives and more biopsies. • The yield of screening in terms of cancer detected declines rapidly with repeated annual testing. If screening were to reduce mortality, biennial PSA screening could yield as much benefit as annual screening.
Rating Scheme	
ACS (2001)	Not applicable
UMHS (2004) New	Levels of evidence reflect the best available literature in support of an intervention or test: A. Randomized controlled trials B. Controlled trials, no randomization C. Observational trials D. Opinion of expert panel
USPSTF (2002)	USPSTF grades its recommendations according to one of five classifications (A, B, C, D, or I), reflecting the strength of evidence and magnitude of net benefit (benefits minus harms). A The USPSTF strongly recommends that clinicians routinely provide [the service] to eligible patients. (The USPSTF found good evidence that [the service] improves important health outcomes and concludes that benefits substantially outweigh harms.) B The USPSTF recommends that clinicians routinely provide [the service] to eligible patients. (The USPSTF found at least fair evidence that [the service] improves health outcomes and concludes that benefits

	outweigh harms.) C The USPSTF makes no recommendation for or against routine provision of [the service]. (The USPSTF found at least fair evidence that [the service] can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.) D The USPSTF recommends against routinely providing [the service] to asymptomatic patients. (The USPSTF found at least fair evidence that [the service] is ineffective or that harms outweigh benefits.) I The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing [the service]. (Evidence that [the service] is effective is lacking, of poor quality, or conflicting and the balance of benefits and harms cannot be determined.) USPSTF grades the quality of the overall evidence on a 3-point scale (good, fair, or poor). Good Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes. Fair Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies; generalizability to routine practice; or indirect nature of evidence on health outcomes. Poor Evidence is insufficient to assess the effects on health outcomes because of limited number of power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

TABLE 3: BENEFITS AND HARMS	
Potential Benefits Associated with Prostate Cancer Screening	
ACS (2001)	Prostate cancer screening may result in the diagnosis of earlier-stage disease in younger men, which may decrease prostate cancer mortality rates. However, no direct evidence exists to show that prostate-specific antigen (PSA) screening decreases prostate cancer mortality rates.
UMHS (2004) New	Early detection and treatment may avert future cancer-related illness.
USPSTF (2002)	Effectiveness of Early Detection USPSTF found one randomized, controlled trial (RCT), and three case-control studies examining the effect of screening on prostate cancer mortality. The single RCT of PSA and DRE screening, which reported a benefit from screening, was hampered by a low rate of acceptance of screening in the intervention group (24%), and by flaws in the published analysis; no difference in prostate cancer deaths was observed between the groups randomized to screening versus usual care using "intention to treat" analysis. Three case-control studies of screening DRE produced mixed results. A number of RCTs of PSA screening for prostate cancer are under way in both the U.S. and Europe, but they are not expected to report results for several years. Data are also limited to determine whether and how much treatment of screen-detected cancers improves outcomes. No properly controlled, prospective studies are available to determine whether prostatectomy or radiation, the most commonly used treatments for prostate cancer, reduce mortality or are more effective than "watchful waiting" for organ-confined prostate cancer. Several such trials are currently under way. In observational studies, outcomes are worst, and the potential impact of aggressive treatment greatest, for poorly differentiated cancers. In the absence of better data on which treatments are effective for which tumors, the USPSTF concluded that it could not determine whether the increased detection of prostate cancer from screening would reduce mortality and morbidity. The USPSTF also examined a variety of ecologic data, including studies of secular trends in prostate cancer mortality after introduction of PSA screening and comparisons of prostate cancer mortality rates in communities with and without screening. Prostate cancer mortality rates in the U.S. have declined since 1991. However, the available ecologic studies have not provided sufficient evidence that prostate cancer trends in the U.S. or other populations are attributable to screening; differences in prostate cancer treatment, underlying risk

	factors, and how deaths are classified can all introduce bias into ecological comparisons.
Potential Harms Associated with Prostate Cancer Screening	
ACS (2001)	Since prostate-specific antigen is prostate-tissue specific and not prostate-cancer specific, there is no absolute value that is applicable to all men. The range of "normal" prostate-specific antigen levels has conventionally been considered to be between zero and 4.0 ng/dl. A lower cut-off value of 2.5 ng/dl has been shown to improve the early detection of organ-confined prostate cancers; however, this also increases the number of men undergoing biopsy in whom no cancer is detected.
UMHS (2004) New	DRE Although DRE can successfully detect some prostate cancers, it is less effective in detecting tumors deep within the prostate gland, and its impact on prostate cancer mortality has been shown to be limited. DRE has a significant subjective component that is manifested by only fair inter-examiner agreement. In addition, it has been suggested that 25 to 35% of prostate cancers occur in areas of the prostate not accessible to the examining finger. The sensitivity of DRE ranges from 18 to 68% with significantly lower specificity. PSA PSA is generally specific to prostate tissue; however, it is not specific to only prostate cancer. Older men may develop benign prostatic hyperplasia which often elevates PSA, and hence, the specificity of PSA decreases with age.
USPSTF (2002)	Evidence about the harms of screening per se is scant. The screening process is likely associated with some increase in anxiety, but the number of men affected and the magnitude of the increased anxiety are largely unknown. Some screening procedures cause transient discomfort. Fewer than 10% of men have ongoing interference with daily activities after biopsy, and fewer than 1% suffer more serious complications, including infections. Screening may result in harm if it leads to treatments that carry side effects without improving outcomes from prostate cancer, especially for cancers that have a lower chance of progressing. Erectile dysfunction, urinary incontinence, and bowel dysfunction are well-recognized and relatively common adverse effects of treatment with surgery, radiation or androgen ablation, but men differ in their responses to these symptoms.

GUIDELINE CONTENT COMPARISON

The American Cancer Society (ACS), the University of Michigan Health System (UMHS), and the U.S. Preventive Services Task Force (USPSTF) present recommendations for screening men for prostate cancer and provide explicit reasoning behind their judgments.

In addition to prostate cancer screening, the UMHS guideline provides screening recommendations for breast cancer, cervical cancer, ovarian cancer, and colorectal cancer (see related cancer screening syntheses).

Areas of Agreement

Routine Screening

All three organizations cite a lack of conclusive evidence that screening can reduce mortality from prostate cancer. ACS recommends against routine screening, while UMHS suggests that clinicians should share decision making regarding screening with the patient, providing the patient with clear information regarding the benefits and risks of screening. USPSTF does not recommend for or against routine screening. All three groups also address the clear potential that screening will increase treatment-related morbidity.

Targeted Screening/Informed Decision-making

As the incidence of prostate cancer increases with age, ACS, UMHS, and USPSTF generally recommend that screening should be offered to men 50 years of age and older with at least a 10-year life expectancy and men less than 50 years of age at risk for developing prostate cancer (e.g., family history, African American). ACS and USPSTF suggest initiating screening of high-risk individuals at 45 years of age, while UMHS suggests 40 years of age.

All three organizations assert that men should make an informed decision regarding prostate cancer screening with the help of their physicians.

Screening Tests

When the decision to screen is made, there is agreement among the groups that PSA and DRE are the primary screening tests for prostate cancer.

The use of transrectal ultrasound as a screening test for prostate cancer is no longer considered by USPSTF. ACS mentions transrectal ultrasound once in their guideline in terms of biopsy. Similarly, UMHS refers to the use of transrectal ultrasound and/or needle biopsy of the prostate, in the context of appropriate follow-up tests for abnormal initial screening tests.

Areas of Differences

Screening Tests

Although there is agreement among all the groups on the use of PSA and DRE as the primary screening tools for prostate cancer, ACS explicitly recommends combining the two to improve accuracy. USPSTF notes that when DRE and PSA are combined, more cancers are detected than when PSA is used alone. They further note, however, that their combined use in screening increases the rate of false-positive results. Contrary to this, UMHS argues that the combined use of DRE and PSA will decrease the rate of false positives (e.g., when both PSA and DRE are suspicious), but at the expense of reduced sensitivity (ability of the combined tests to identify patients with prostate cancer).

There is variation among the three organizations regarding the best methods to improve PSA sensitivity and specificity. All agree that a PSA threshold level of 4.0 ng/dl will detect many cancers but that as many as 10% to 20% may be missed. ACS discusses age-specific reference ranges, PSA density, and free-to-total PSA ratios, suggesting the latter method be used to increase testing accuracy in certain scenarios. UMHS likewise notes that, because of age-related changes in PSA levels, age-adjusted reference ranges may increase the clinical utility of PSA testing. USPSTF does not make recommendations specifically for any of these methods noting that there is insufficient evidence that these variations will improve the accuracy of screening in practice. They further add that using a lower threshold to define an abnormal PSA will detect more cancers, but at the cost of more false positives and more biopsies.

Frequency of Targeted Screening

ACS is the only group that specifically recommends annual screening for men over 50 and younger men who are at increased risk. UMHS, while not making explicit recommendations for annual screening, suggests that physicians begin offering screening (involving patients in the decision making process) at 50 years of age for average-risk patients, or at 40 years for high-risk individuals., In contrast, USPSTF reports that cancer detection declines rapidly with repeated annual testing and suggests biennial screening as equally effective, if screening were to reduce mortality.

This Synthesis was prepared by NGC on December 28, 1998 and has been revised a number of times. The most current version of this Synthesis incorporates new guidelines from UMHS and removes recommendations of the American Urological Association (2000) and Singapore Ministry of Health (2000). The information was verified by UMHS on August 23, 2005.

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